REMARKS

I. Status of the Claims

With entry of this amendment, claims 4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 39, and 40-56 are pending in this application. The rejection of claims 4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 39 under 35 U.S.C. § 112, first paragraph, as allegedly being nonenabling is withdrawn. Advisory Action, at page 2. Claims 4, 5, 7, 21, 23, 25, 27, 31, 33, and 39 stand rejected under 35 U.S.C. § 102. Claim 4 has been amended. Claims 40-56 have been added. Support for amended claim 4 can be found, for example, on page 7, paragraph 25, of the as-filed specification. Support for the new claims can be found in the previously canceled claims and in the as-filed specification. No new matter is added by this amendment.

II. The Claims Are Not Anticipated

The Examiner maintains the rejection of claims 4, 5, 7, 21, 23, 25, 27, 31, 33, and 39 under 35 U.S.C. § 102(b) as allegedly being anticipated by Kuo *et al.* (Development, 126:4223-4234, 1999). Advisory Action, at page 2. According to the Examiner, "the 213 bp fragment of the mouse CARP promoter, between nucleotides –166 and +47, which confers cardiac specific expression, disclosed by Kuo et al. consists of a fragment of SEQ ID NO:2." *Id.* The Examiner concludes "[t]he disclosure of Kuo et al. meets all the structural limitations of the claims, and therefore is considered to possess the functional limitations of the claim, namely to [sic, the] ability to induce cardiac-specific expression in vivo, absent evidence to the contrary." *Id.*

Applicants respectfully traverse. In order to anticipate a claim, a reference must teach every element of the claim. M.P.E.P. § 2131. Here, each rejected claim depends (directly or indirectly) on claim 4, which recites, *inter alia*,. "[a] polynucleotide comprising a fragment of SEQ ID NO: 2 [human CARP] or a fragment having at least 90% sequence identity to a fragment of SEQ ID NO: 2, wherein said polynucleotide . . . specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide."

None of the constructs tested by Kuo *et al.* have the properties recited by claim 4. As Applicants have previously noted, Kuo *et al.* tested the transcriptional activity of certain sequences upstream of the ***mouse, not the human, CARP gene***. Amendment After Final filed September 28, 2004, at page 9. Nevertheless, the Examiner asserts that "the 213 bp fragment of the mouse CARP promoter, between nucleotides –166 and +47" both "confers cardiac specific expression" and "consists of a fragment of SEQ ID NO:2." Advisory Action, at page 2.

Neither statement is true. According to Kuo *et al.*, the fragment the Examiner relies on shows activity only when present as a tandem repeat with nucleotides –166 to -39 of the mouse CARP gene. *See* Figure 3 (p2x0.128TATA Luc). Clearly, this tandem repeat cannot credibly be characterized as either a fragment of SEQ ID NO: 2 or a fragment with 90% (or even 80%) identity to SEQ ID NO: 2. In fact, the tandem repeat could not even be reasonably called a fragment of the mouse CARP gene. Kuo *et al.* show that a slightly longer fragment of the mouse CARP gene, p0.176Luc, which has

78.9% identity to a fragment of SEQ ID NO: 2 (*see* Exhibit A), has no activity. *See* Figure 3.

A third fragment of the mouse CARP gene tested by Kuo *et al.*, p0.295Luc, does have promoter activity and shows 83.0% identity to a fragment of SEQ ID NO: 2. *See* Kuo *et al.*, Figure 3; Exhibit B. Kuo *et al.* do not disclose that this fragment "specifically induces expression in cardiac cells *in vivo*" as recited by claim 4. *See* Kuo *et al.*, at page 4227 (reporting that expression of a β-galactosidase transgene from the p0.295lacZ construct in embryos was observed in the myocardium and in somites and that there was no detectable expression in adult hearts). Solely to advance prosecution, however, Applicants have amended claim 4 to recite "or a fragment having at least 90% sequence identity to a fragment of SEQ ID NO: 2." As noted above, the mouse sequence in p0.295Luc and p0.295lacZ has only 83.0% identity to a fragment of SEQ ID NO: 2 and, for this reason alone, cannot anticipate claim 4 or claims 5, 7, 21, 23, 25, 27, 31, 33, and 39, which depend therefrom.

Moreover, the longer fragments of the mouse CARP gene promoter tested by Kuo *et al.* do not anticipate the claims for at least two reasons. First, as the size of the mouse CARP gene fragment increases, its percent identity with SEQ ID NO: 2 decreases. Thus, when 1.2 kbp of the mouse CARP promoter are aligned with SEQ ID NO: 2, the identity is 64%; when the comparison is to 1.5 kbp of the mouse CARP promoter, the percent identity is 60%; and when 2.5 kbp of the mouse CARP gene promoter is aligned with SEQ ID NO: 2, the percent identity drops to 52%. In other

words, larger fragments of the mouse CARP gene promoter are not 90% identical to a fragment of SEQ ID NO: 2.

Second, Kuo *et al.* describe only nucleotides –299 to +62 of the mouse CARP gene, *see* Figure 2D, and, under *Regents of the University of California v. Eli Lilly & Co.* 43 U.S.P.Q.2d 1398, 1404 (Fed. Cir. 1997), cannot anticipate claims to fragments containing nucleotide sequences outside this region. As the Examiner correctly noted, "the Lilly decision concerns those rejections made under 35 U.S.C. 112, first paragraph for written description, and not 35 U.S.C. 102 rejections for anticipation." Advisory Action, at page 2. However, in order to anticipate a claim, a reference, in addition to being prior art, "must be enabling and ***describe the applicant's claimed invention sufficiently*** to have placed it in possession of a person of ordinary skill in the field of the invention." *In re Paulsen*, 30 F.3d 1475 (Fed. Cir. 1994) (emphasis added). Here, because Kuo *et al.* provide no description of the sequences upstream of nucleotide –299 of the mouse CARP gene, that reference cannot anticipate fragments of SEQ ID NO: 2 containing such sequences.

For the reasons above, Applicants respectfully request the reconsideration and withdrawal of the rejection of claims 4, 5, 7, 21, 23, 25, 27, 31, 33, and 39 under 35 U.S.C. § 102(b) as anticipated by Kuo *et al.*

III. New Claims 40-56 Are Patentable

The Examiner previously asserted that claims reciting fragments of SEQ ID NO: 1 were anticipated by Kuo *et al.* and by Chien *et al.*, (WO 00/15821). New claims 40-56

are drawn to a polynucleotide comprising SEQ ID NO: 1 or a sequence having at least 93% identity to SEQ ID NO: 1. The polynucleotide disclosed in Chien *et al.* shares only 90% identity with the complete sequence of SEQ ID NO: 1 of the present invention (in part, because of a 111 bp insertion found in SEQ ID NO: 1 but not in the polynucleotide of Chien *et al.*). Applicants respectfully submit that the new claims are not anticipated by Chien *et al.* because the sequence disclosed by Chien *et al.* is not the exact same sequence of SEQ ID NO: 1 or a sequence that is 93% identical to SEQ ID NO: 1.

Nor does the sequence reported by Kuo *et al.* anticipate the new claims. As noted above, Kuo *et al.* describes only nucleotides –299 to +62 of the mouse CARP gene. Based on *Regents of the University of California v. Eli Lilly & Co.* and *In re Paulsen*, Kuo *et al.* cannot anticipate a polynucleotide comprising SEQ ID NO: 1 because it fails to provide sufficient description of the chemical structure of SEQ ID NO: 1, which contains 2358 nucleotides.

For the reasons above, Applicants respectfully request the timely allowance of claims 40-56.

IV. Conclusion

In view of the foregoing amendment and remarks, Applicants respectfully request the continued examination of this application pursuant to 37 C.F.R. § 1.114, and the timely allowance of the pending claims. Should the Examiner feel that this application is not in condition for allowance, Applicants request that she contact their undersigned representative at 202-408-4185.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: February 28, 2005

By: _____
William L. Strauss
Reg. No. 47,114

Attachments: **Exhibit A (Alignment of SEQ ID NO: 2 with p0.176Luc)**
Exhibit B (Alignment of SEQ ID NO: 2 with p0.295Luc)

Exhibit A

NCBI BLAST 2 Sequences Results (Version BLASTN 2.2.10)

p0.176Luc (-176 to +47) of Kuo et al. aligned with SEQ ID NO: 2

Identities = 176/223 (78.9%)

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Query[1]:  -176 ccgcggccagcttgtcatctccctcttgggcttcccagacactaagtctggaatgaaaattcacctgcctctgaattg
                |    |   |  ||  |||||||||  |||||||||||||| |||||||||||||||||||||||||||||| |||
Sbjct[2]:  1838 gggttagcttgtcctcccctccctcttcagcttcccagacactgagtctggaatgaaaattcacctgcctctgagttg

gccactggtgggggcaggggtgtgacttggcttcccaggctggaagattatctcacccagccctagctatataa-cgggctggtgtggag
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gctcctaatgggggcgggagtgttacttcggttcccaggttggaagattatctcacccggccccagctatataagctgaccggtgtggag

gggctccacagggccagttccaggggttcatccacaagagagaaaaacatagactc +47
||||  |  ||||||||  |||||||| |||  |  |  ||  ||  |||||||||||  |
gggcccagcagggccaactccagggattccttc-cacgacagaaaaacatacaaga  2060
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[1] Sequence of the 5' flanking region of the mouse CARP gene (*See* Figure 2D in Kuo *et al.* (Development, 126:4223-4234, 1999).

[2] Sequence of SEQ ID NO: 2 in U.S. Patent Application No.: 10/005,337

Exhibit B

NCBI BLAST 2 Sequences Results (Version BLASTN 2.2.10)

p0.295Luc (-295 to +47) of Kuo et al. aligned with SEQ ID NO: 2

Identities = 284/342 (83.0%)

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Query[1]:  -295 gcaatattaacaggcagctgtcccctggcttcccgatacgtgggatgactcgcattgctgagcggtgtggtcact
               ||||| | ||||| |||||||||||||| || |  || |  | |||||||| |||||||||||||| |||| ||||
Sbjct[2]:  1715 gcaatgtcaacagacagctgtcccctgact-cttgacaaataggatgacttgcattgctgagcgatgtgatcacc

gccaaaggaatgaccctctcacatttcttcctgattcgcatacgccgc--ggccagcttgtcatc---tccctcttgggcttcccagac
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accaaaggaatggccctctcacatttcttcctgattcacatattcagcagggttagcttgtcctcccctccctcttcagcttcccagac

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ctcacccagccctagctatataa-cgggctggtgtggaggggctccacagggccagttccaggggttcatccacaagagagaaaaacata +47
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ctcacccggccccagctatataagctgaccggtgtggaggggcccagcagggccaactccagggattccttc-cacgacagaaaaacata  2060
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[1] Sequence of the 5' flanking region of the mouse CARP gene (*See* Figure 2D in Kuo *et al.* (Development, 126:4223-4234, 1999).

[2] Sequence of SEQ ID NO: 2 in U.S. Patent Application No.: 10/005,337